

LISTING OF THE CLAIMS:

This listing of the claims will replace all prior versions, and listings, of the claims in the present application.

Claims 1-24 (canceled)

25. (currently amended) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof; ~~and~~  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,

wherein ~~means for providing~~ the mean fasting plasma concentration ~~vs.~~ versus time curve of Figure 14 is achieved upon single administration of the sustained release oral dosage form to human subjects.

26. (currently amended) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof; ~~and~~  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,

wherein ~~means for providing~~ the mean fed plasma concentration ~~vs.~~ versus time curve of Figure 14 is achieved upon single administration of the sustained release oral dosage form to human subjects.

27. (currently amended) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof; ~~and~~  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,

wherein ~~means for providing~~ the mean fasting plasma concentration ~~vs.~~ versus time curve of Figure 15 is achieved upon single administration of the sustained release oral dosage form to human subjects.

28. (currently amended) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof; ~~and~~  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,

wherein ~~means for providing~~ the mean fed plasma concentration ~~vs.~~ versus time curve of

Figure 15 is achieved upon single administration of the sustained release oral dosage form to human subjects.

29. (currently amended) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof; ~~and~~  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,

~~wherein means for providing~~ the mean plasma concentration ~~vs.~~ versus time curve of Figure 16 is achieved upon steady state administration of the sustained release oral dosage form to human subjects.

30. (currently amended) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof; ~~and~~  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,

~~wherein means for providing~~ the mean fasting plasma concentration ~~vs.~~ versus time curve of Figure 17 is achieved upon single administration of the sustained release oral dosage form to human subjects.

31. (currently amended) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof; ~~and~~  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,

~~wherein means for providing~~ the mean fed plasma concentration ~~vs.~~ versus time curve of Figure 17 is achieved upon single administration of the sustained release oral dosage form to human subjects.

32. (previously presented) The dosage form of claim 25, wherein said dosage form comprises hydromorphone hydrochloride.

33. (previously presented) The dosage form of claim 26, wherein said dosage form comprises hydromorphone hydrochloride.

34. (previously presented) The dosage form of claim 27, wherein said dosage form comprises hydromorphone hydrochloride.

35. (previously presented) The dosage form of claim 28, wherein said dosage form comprises hydromorphone hydrochloride.
36. (previously presented) The dosage form of claim 29, wherein said dosage form comprises hydromorphone hydrochloride.
37. (previously presented) The dosage form of claim 30, wherein said dosage form comprises hydromorphone hydrochloride.
38. (previously presented) The dosage form of claim 31, wherein said dosage form comprises hydromorphone hydrochloride.
39. (new) A sustained release oral dosage form comprising an extruded blend of:  
a first therapeutic agent consisting of an opioid analgesic;  
a second therapeutic agent consisting of one or more non-opioid therapeutic agents;  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,  
wherein said extruded blend is extruded through an extruder to form an extrudate comprising of a strand-shaped matrix cut into multi-particulates having a length of from about 0.1 to about 5 mm and a diameter of from about 0.1 to about 5 mm.
40. (new) The dosage form of claim 39, wherein said opioid analgesic is alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, bupernorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dexocine, diampromide, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl, butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl morphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, pharmaceutically acceptable salts thereof, or a combination thereof.
41. (new) The dosage form of claim 39, wherein said opioid analgesic is morphine, codeine, hydromorphone, hydrocodone, oxycodone, oxymorphone, dihydrocodeine,

dihydromorphine, tramadol, pharmaceutically acceptable salts thereof, or a combination thereof.

42. (new) The dosage form of claim 39, wherein said opioid analgesic consists of from about 2 mg to about 64 mg hydromorphone hydrochloride.

43. (new) The dosage form of claim 39, wherein said opioid analgesic consists of from about 5 mg to about 800 mg morphine.

44. (new) The dosage form of claim 39, wherein said opioid analgesic consists of from about 5 mg to about 400 mg oxycodone.

45. (new) The dosage form of claim 39, wherein said opioid analgesic consists of from about 50 mg to about 800 mg tramadol.

46. (new) The dosage form of claim 39, wherein said non-opioid therapeutic agent is a non-steroidal anti-inflammatory agent.

47. (new) The dosage form of claim 39, wherein said non-opioid therapeutic agent is ibuprofen, diclofenac, naproxen, benoxaprofen, flurbiprofen, fenoprofen, flubufen, ketoprofen, indoprofen, piroprofen, carprofen, oxaprozin, pramoprofen, muprofen, trioxaprofen, suprofen, aminoprofen, tiaprofenic acid, fluprofen, bucloxic acid, indomethacin, sulindac, tolmetin, zomepirac, tiopinac, zidometacin, acetaminophen, fentiazac, clidanac, oxpinac, mefenamic acid, meclofenamic acid, flufenamic acid, niflumic acid, tolfenamic acid, diflurisal, flufenisal, piroxicam, sudoxicam, isoxicam, acetaminophen, aspirin, salicylate-derived analgesics and antipyretics, pharmaceutically acceptable salts thereof, or a combination thereof.

48. (new) The dosage form of claim 39, wherein said non-opioid therapeutic agent is incorporated as a separate controlled release layer.

49. (new) The dosage form of claim 39, wherein said non-opioid therapeutic agent is incorporated as an immediate release layer.

50. (new) The dosage form of claim 39, wherein said non-opioid therapeutic agent is incorporated into the controlled release matrix along with the opioid.

51. (new) The dosage form of claim 39, wherein said non-opioid therapeutic agent is incorporated in a capsule with extrudates comprising the opioid analgesic.
52. (new) The dosage form of claim 39, wherein said hydrophobic material is alkylcelluloses, acrylic and methacrylic acid polymers and copolymers, shellac, zein, hydrogenated castor oil, hydrogenated vegetable oil, or a combination thereof.
53. (new) The dosage form of claim 39, wherein said hydrophobic fusible carrier is natural waxes, synthetic waxes, fatty alcohols, fatty acids, fatty acid esters, fatty acid glycerides, hydrogenated fats, hydrocarbons, stearic acid, stearyl alcohol, hydrophobic and hydrophilic polymers having hydrocarbon backbones, or a combination thereof.
54. (new) The dosage form of claim 39, wherein the blend is subjected to a sufficient amount of heat to at least soften said blend during the extrusion process.
55. (new) The dosage form of claim 39, wherein a unit dose comprising an effective amount of said extrudate is contained within a gelatin capsule.
56. (new) The dosage form of claim 39, wherein a unit dose comprising an effective amount of said extrudate is compressed into a tablet.
57. (new) The dosage form of claim 39, which provides a peak plasma level of said opioid analgesic from about 2 to about 8 hours after oral administration.
58. (new) The formulation of claim 39, which provides an *in-vitro* release of the opioid analgesic when assessed by the USP Paddle or Basket Method at 100 rpm at 900 ml aqueous buffer (pH between 1.6 and 7.2) at 37°C from about 1 to about 42.5% opioid release after one hour, from about 5 to about 65% opioid released after 2 hours, from about 15 to about 85% opioid released after 4 hours, from about 20 to about 90% opioid released after 6 hours, from about 35 to about 95% opioid released after 12 hours, from about 45 to about 100% opioid released after 18 hours, and from about 55 to about 100% opioid released after 24 hours, by weight.
59. (new) The dosage form of claim 39, which provides a rapid rate of initial rise in the plasma concentration of the opioid analgesic after oral administration, such that the absorption half-life is from about 1 to about 8 hours after oral administration.

60. (new) The dosage form of claim 39, which provides an *in-vitro* release when assessed by the USP Paddle or Basket Method at 100 rpm at 900 ml aqueous buffer (pH between 1.6 and 7.2) at 37°C from about 12.5 to about 42.5% opioid released after one hour, from about 25 to about 65% opioid released after 2 hours, from about 45 to about 85% opioid released after 4 hours, and greater than about 60% opioid released after 8 hours, by weight.

61. (new) The dosage form of claim 39, wherein said opioid analgesic, the one or more hydrophobic materials, and the one or more hydrophobic fusible carriers enter said extruder in powder form.

62. (new) The dosage form of claim 39, wherein the opioid analgesic is released for a time period of from about 8 to about 24 hours.

63. (new) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof;  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,  
wherein the mean amount of hydromorphone or a pharmaceutically acceptable salt thereof absorbed is about 19 ng hr/ml,  $C_{\max}$  is about 0.72 ng/ml and  $T_{\max}$  is about 6.8 hours, upon single administration of the sustained release oral dosage form to fasted human subjects.

64. (new) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof;  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,  
wherein the mean amount of hydromorphone or a pharmaceutically acceptable salt thereof absorbed is about 20.10 ng hr/ml,  $C_{\max}$  is about 0.75 ng/ml and  $T_{\max}$  is about 2.4 hours, upon single administration of the sustained release oral dosage form to fed human subjects.

65. (new) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof;  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,  
wherein the mean amount of hydromorphone or a pharmaceutically acceptable salt thereof absorbed is about 19.23 ng hr/ml,  $C_{\max}$  is about 0.76 ng/ml and  $T_{\max}$  is about 3.9 hours, upon single administration of the sustained release oral dosage form to fasted human subjects.

66. (new) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof;  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,  
wherein the mean amount of hydromorphone or a pharmaceutically acceptable salt thereof  
absorbed is about 21.47 ng hr/ml,  $C_{\max}$  is about 0.93 ng/ml and  $T_{\max}$  is about 1.9 hours, upon  
single administration of the sustained release oral dosage form to fed human subjects.

67. (new) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof;  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,  
wherein the mean amount of hydromorphone or a pharmaceutically acceptable salt thereof  
absorbed is about 36.08 ng hr/ml,  $C_{\max}$  is about 2.15 ng/ml and  $T_{\max}$  is about 5.8 hours, upon  
single administration of the sustained release oral dosage form to human subjects.

68. (new) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof;  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,  
wherein the mean amount of hydromorphone or a pharmaceutically acceptable salt thereof  
absorbed is about 15.83 ng hr/ml,  $C_{\max}$  is about 0.52 ng/ml and  $T_{\max}$  is about 5.6 hours, upon  
single administration of the sustained release oral dosage form to fasted human subjects.

69. (new) A sustained release oral dosage form comprising:  
hydromorphone or a pharmaceutically acceptable salt thereof;  
one or more hydrophobic materials; and  
one or more hydrophobic fusible carriers,  
wherein the mean amount of hydromorphone or a pharmaceutically acceptable salt thereof  
absorbed is about 16.55 ng hr/ml,  $C_{\max}$  is about 0.65 ng/ml and  $T_{\max}$  is about 4.1 hours, upon  
single administration of the sustained release oral dosage form to fed human subjects.